ABSTRACT

Acetaminophen (APAP) overdose causes severe liver and kidney damage. APAP-induced liver injury (AILI) represents the most frequent cause of drug-induced liver failure. APAP is relatively insoluble and can only be taken orally; however, its prodrug, propacetamol, is water soluble and usually injected directly. In this study, we examined the time-dependent effects of AILI after propacetamol injection in mice. After analyses of alanine aminotransferase and aspartate aminotransferase activities and liver histopathology, we demonstrated that a novel AILI mouse model can be established by single propacetamol injection. Furthermore, we compared the protective and therapeutic effects of galangin with a known liver protective extract, silymarin, and the only clinical agent for treating APAP toxicity, N-acetylcysteine (NAC), at the same dose in the model mice. We observed that galangin and silymarin were more effective than NAC for protecting against AILI. However, only NAC greatly improved both the survival time and rate consequent to a lethal dose of propacetamol. To decipher the hepatic protective mechanism(s) of galangin, galangin pretreatment significantly decreased the hepatic oxidative stress, increased hepatic glutathione level, and decreased hepatic microsomal CYP2E1 levels induced by propacetamol injection. In addition, propacetamol injection also reproduced the probability of APAP-induced kidney injury (AIKI), appearing similar to a clinical APAP overdose. Only galangin pretreatment showed the protective effect of AIKI. Thus, we have established a novel mouse model for AILI and AIKI using a single propacetamol injection. We also demonstrated that galangin provides significant protection against AILI and AIKI in this mouse model.

Keywords: galangin, liver and kidney protections, n-acetylcysteine, novel drug overdose mouse models, p...